ERODIUM CRASSIFOLIUM L'HER PLANT EXTRACTS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is also a continuation-in-part of U.S. patent application Ser. No. 15/563,595, filed Oct. 1, 2017, titled "*ERODIUM CRASSIFOLIUM* L'HER PLANT EXTRACTS AND USES THEREOF", which is a national phase of International Patent Application No. PCT/IL2016/050348, filed Mar. 31, 2016, titled "*ERODIUM CRASSIFOLIUM* L'HER PLANT EXTRACTS AND USES THEREOF", which claims the benefit of priority of U.S. Provisional Patent Application No. 62/141,313, filed Apr. 1, 2015, titled "DEVELOPMENT OF THERAPEUTIC/NUTRITIONAL PRODUCTS BASED ON *ERODIUM CRASSIFOLIUM* L'HER PLANT EXTRACTS".

[0002] The contents of all the above applications are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

[0003] The present invention, in some embodiments, relates to extracts of *Erodium* plants and, more particularly, but not exclusively, to polar extracts of tubers of *Erodium* plants.

BACKGROUND OF THE INVENTION

[0004] From an ethnobotanical perspective, many plants from the Geraniaceae family are considered to have medicinal value. In particular, some of the species belonging to the genus *Erodium* of this family have recognized medicinal applications known from folklore and empirical data. *Erodium* species are used to treat a variety of human ailments such as colds, coughs, diarrhea, hemorrhaging and are used to dress wounds. One of the species, *Erodium botrys* is known from the ethnobotanical explorations conducted by the British anthropologist Melville William Hilton-Simpson (1881-1938) as a traditional dressing for wounds.

[0005] *Erodium crassifolium* L'Her (Hairy storks bill) is a hemicryptophyte (i.e. buds at or near the soil surface). It develops tubers on its roots. It has a suffruticose branching stem and flowering branches which are erect, slender, reddish brown, and thickly clothed with unequal villous hairs. Its leaves are alternate, rosette, pinnated or deeply lacinated. The flowers of this plant are hermaphrodite; pink and violet. The plant habitat is shrub-steppes and desert (FIG. **1**). *Erodium crassifolium* L'Her is common in the Negev Highlands of Israel, with less than 90 mm annual precipitation. The plant produces a small tuber in the ground about 20 cm deep. This organ serves as a water and nutrient reservoir enabling the plant to overcome the dry season (FIG. **1**). It is traditionally known that the tubers are edible, used mainly by the Bedouin nomadic tribes. The tubers have a sweet taste and are best in late winter or early spring when they are whitish in color.

[0006] Traditional knowledge considers the tubers useful in the treatment of epilepsy and some skin disorders, including insect bites (http://www(dot)cretanflora(dot)com/*erodium_crassifolium*(dot)html).

[0007] Due to the traditional uses of *E. crassifolium*, the inventors are interested in examining its anti-oxidant and anti-inflammatory activities in vitro on a skin model.

SUMMARY OF THE INVENTION

[0008] The present invention, in some embodiments, discloses the measuring of anti-inflammatory activity of *Erodium* extracts, by quantifying the level of interleukin-8 (IL-8), a pro-inflammatory chemokine involved in inflammation, including in skin diseases.

[0009] In some embodiments, the present invention is based, in part, on the finding the *E. crassifolium* tuber ethanol extract (EE) and its fractions, induced a significant in vitro anti-inflammatory activity on normal keratinocyte cell line (HaCaT). Further, the inventors have identified some of the active compounds, and accordingly, suggest that the EE in vitro anti-inflammatory activity may be attributed to a combination of these compounds.

[0010] According to a first aspect, there is provided a composition consisting essentially of: epigallocatechin, mannofuranose, α-D-xylopyranose, gallic acid, palmitic acid, stearic acid, trans-catechin, cis-catechin, and an acceptable carrier.

[0011] According to another aspect, there is provided a method for treating a subject afflicted with an inflammatory or a condition associated therewith, comprising administering to the subject a therapeutically effective amount of the composition of the invention.

[0012] In some embodiments, epigallocatechin is present in an amount of 35-50% (w/w) of the composition.

[0013] In some embodiments, mannofuranose is present in an amount of 15-22% (w/w) of the composition.

[0014] In some embodiments, α-D-xylopyranose is present in an amount of 1.5-3.5% (w/w) of the composition.

[0015] In some embodiments, gallic acid is present in an amount of 3-7% (w/w) of the composition.

[0016] In some embodiments, palmitic acid is present in an amount of 4-8% (w/w) of the composition.

[0017] In some embodiments, stearic acid is present in an amount of 0.5-3.5% (w/w) of the composition.

[0018] In some embodiments, trans-catechin is present in an amount of 8-15% (w/w) of the composition.

[0019] In some embodiments, cis-catechin is present in an amount of 7-16% (w/w) of the composition.

[0020] In some embodiments, any one of the: epigallocatechin, mannofuranose, α-D-xylopyranose, gallic acid, palmitic acid, stearic acid, trans-catechin, and cis-catechin, is derived from a polar extract of *Erodium* plant tuber.

[0021] In some embodiments, the polar solvent comprises 50-90% (v/v) ethanol.

[0022] In some embodiments, the *Erodium* plant is *Erodium crassifolium* L'Her.

[0023] In some embodiments, the composition is a pharmaceutical composition or a nutraceutical composition.

[0024] In some embodiments, the composition is suitable for topical administration or oral administration.

[0025] In some embodiments, the inflammatory disease comprises an inflammatory skin disease.

[0026] In some embodiments, the skin disease is selected from the group consisting of: a cutaneous disease, a dermal disease, a bullous skin disease, *Pemphigus vulgaris*, bullous pemphigoid, *Pemphigus foliaceus*, and any combination thereof.

[0027] In some embodiments, the inflammatory disease is induced by irradiation, oxidative stress, or both.

[0028] In some embodiments, treating comprises reducing the expression level, the activity, or both, of interleukin 8